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Effects of dehydration on cerebrovascular control during standing after heavy resistance exercise

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Moralez G, Romero SA, Rickards CA, Ryan KL, Convertino VA, Cooke WH. Effects of dehydration on cerebrovascular control during standing after heavy resistance exercise. *J Appl Physiol* 112: 1875–1883, 2012. First published March 29, 2012; doi:10.1152/japplphysiol.01217.2011.—We tested the hypothesis that dehydration exacerbates reductions of middle cerebral artery blood velocity (MCAv) and alters cerebrovascular control during standing after heavy resistance exercise. Ten males participated in two trials under *1*) euhydration (EUH) and *2*) dehydration (DEH; fluid restriction + 40 mg furosemide). We recorded finger photoplethysmographic arterial pressure and MCAv (transcranial Doppler) during 10 min of standing immediately after high-intensity leg press exercise. Symptoms (e.g., lightheadedness) were ranked by subjects during standing (1–5 scale). Low-frequency (LF) oscillations of mean arterial pressure (MAP) and mean MCAv were calculated as indicators of cerebrovascular control. DEH reduced plasma volume by 11% ($P = 0.002$; calculated from hemoglobin and hematocrit). During the first 30 s of standing after exercise, subjects reported greater symptoms during DEH vs. EUH ($P = 0.05$), but these were mild and resolved at 60 s. While MAP decreased similarly between conditions immediately after standing, MCAv decreased more with DEH than EUH ($P = 0.02$). With prolonged standing under DEH, mean MCAv remained below baseline ($P \leq 0.01$), and below EUH values ($P \leq 0.05$). LF oscillations of MAP were higher for DEH at baseline and during the entire 10 min of stand after exercise ($P \leq 0.057$), while LF oscillations in mean MCAv were distinguishable only at baseline and 5 min following stand ($P = 0.05$). Our results suggest that mean MCAv falls below a "symptomatic threshold" in the acute phase of standing after exercise during DEH, although symptoms were mild and transient. During the prolonged phase of standing, increases in LF MAP and mean MCAv oscillations with DEH may help to maintain cerebral perfusion despite absolute MCAv remaining below the symptomatic threshold.

hypohydration; cerebral blood flow; weight training; cerebrovascular control

PRESERVATION OF CEREBRAL PERFUSION is essential for maintaining consciousness. Heavy resistance exercise poses unique challenges to the maintenance of cerebral perfusion during and after exercise due to rapid and large increases in arterial pressures. For example, during the concentric phase of heavy leg press exercise, arterial pressures may increase three- to fourfold (25). Because cerebrovascular control mechanisms require about 3–5 s to buffer pressure-driven changes in cerebral blood flow (1), oscillations of middle cerebral artery blood velocity (MCAv) mirror those of mean arterial pressure (MAP) during resistance exercises (14, 29, 34). At the cessation of leg press exercise when subjects move from the recumbent to upright position, MCAv decreases acutely to below-baseline levels (34). Such abrupt drops in MCAv could put athletes at risk for pre- or even frank syncope (7) due to inadequate cerebral perfusion and oxygenation (23).

To complicate matters, athletes in weight-class sports such as wrestling and boxing often incorporate voluntary dehydration, in conjunction with vigorous exercise, to make weight for their specific weight class (21). Wrestlers often lose 5% or more of their body weight using such techniques (38). Dehydration results in exaggerated MCAv reductions upon standing (5), and these reductions may be even greater if cerebral regulatory capacity has already been compromised with heavy resistance exercise.

The combination of dehydration and heavy resistance exercise could decrease cerebral perfusion pressures during standing immediately after exercise, contributing to postexercise orthostatic instability. However, the influence of dehydration on cerebrovascular control during standing after heavy resistance exercise is unknown. Therefore, the purpose of this study was to test the hypothesis that voluntary dehydration exacerbates reductions of MCAv acutely, alters cerebrovascular control, and ultimately reduces orthostatic performance as indicated by increased symptoms during prolonged standing after heavy resistance exercise.

METHODS

Subjects. Ten healthy male volunteers with a mean age of 24 ± 2 yr, height of 174 ± 6 cm, and weight of 77 ± 7 kg participated in this study. Subjects were deemed healthy via a PAR-Q questionnaire, were not taking any medications, and did not smoke. Subjects were asked to abstain from caffeine, exercise, and alcohol 24 h before each experimental session due to possible influences on cardiovascular and cerebrovascular regulatory mechanisms. Subjects also received familiarization training with the experimental protocol and procedures before any experiments were performed. The study was approved by the Institutional Review Board for the Protection of Human Subjects in Research at the University of Texas at San Antonio. Written informed consent was obtained from all subjects. Based on changes in MCAv expected during standing after resistance exercise (34), and using a Student's *t*-test-based power calculation, we estimated that a sample size of 10 subjects would be adequate to test our hypothesis with an alpha = 0.05 and a beta = 0.8.

Experimental protocol. Subjects arrived at the laboratory after fasting overnight. A standardized breakfast was given to the subjects 2 h before experimental procedures to avoid fatigue during exercise due to diet restriction. For each of the hydration conditions, subjects reported to the laboratory on 2 consecutive days, a screening day (*session 1*) and an experimental day (*session 2*). Subjects reported to the laboratory for *session 1* at 5:00 PM the afternoon before *session 2*. Prehydration assessment, estimation of six repetition maximum (6

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RM), and protocol familiarization occurred during this session. Measurement of body mass and urine specific gravity, as well as collection of venous blood occurred during the hydration assessment under both hydration conditions. Subjects were weighed wearing the same shorts and T-shirt on all occasions; body mass measurements were obtained using a calibrated weight scale (Tanita Body Composition Analyzer BF-350; Tokyo, Japan). Urine specific gravity was measured on all subjects to confirm euhydration (EUH); subjects provided a urine sample (~100 ml), which was analyzed for excreted concentration of particles, and EUH was confirmed if urine specific gravity was <1.020 g/ml (36). To assess relative changes in blood and plasma volume, blood was collected though venipuncture of an antecubital vein. Duplicate blood samples were immediately transferred into microcuvettes and placed in an automated hemoglobin (Hb) analyzer (Hemocue Hb 201+; Ängelholm, Sweden). They were analyzed for Hb concentration within 5 min of acquisition at ambient room temperature (~21°C). Hematocrit (Hct) was also measured in duplicate. Whole blood samples (~9 μl) were transferred to heparinized microcapillary tubes and consequently analyzed by an automated system (HemataSTAT-II) following microcentrifugation. Hb and Hct were used to calculate percent changes in plasma volume according to the equation of Dill and Costill (13). To establish the exercise test load, subjects performed sets of six repetitions with progressively increasing weight on a recumbent leg press machine (Cybex, Midway, MA) until their 6 RM was attained. Eighty-five percent of a subject's 6 RM was taken as the subject's estimated 10-repetition maximum (10 RM).

Following *session 1*, subjects were instructed to follow one of the two hydration protocols beginning at 8:00 PM the same evening. The orders of the hydration protocols [dehydration (DEH) or EUH] were counterbalanced. The EUH protocol required subjects to maintain hydration status by drinking 0.02 l/kg body mass of water during the 12 h prior to returning to the laboratory (36). In the DEH protocol subjects took 40 mg of the diuretic furosemide at 8:00 PM and then did not ingest any liquids or food for the next 12 h. For both hydration conditions, subjects returned to the laboratory for *session 2* at 8:00 A.M. the next morning for posthydration assessment and lower body resistive exercises. All subjects attended their separate hydration protocol sessions on the same day of the week and at the same time of the day. Hydration protocol sessions were separated by 1 wk, during which time subjects maintained their normal exercise and diet regimen.

Instrumentation and lower body resistive exercise protocol. On the experimental day (*session 2*), following posthydration assessment, subjects warmed up on a stationary cycle ergometer (Monark Ergomedic 839E) for 5 min. Subjects were then seated in the leg press machine and instructed to perform 8–10 practice warm-up repetitions with the weight equivalent to 30% of their estimated 10 RM. Following the warm-up, subjects were instrumented with a three-lead ECG (Harvard apparatus, Holliston, MA) to monitor heart rate (HR). Beat-to-beat arterial blood pressure measurements were obtained from the finger by photoplethysmography (Finometer, Finapres Medical Systems, Amsterdam, The Netherlands). To quantify changes in cerebral blood velocity, a 2-MHz transcranial Doppler ultrasound probe fixed at a constant angle was used to insonate the left MCA over the temporal window (MultiDop T, DWL Electronics, Sipplingen, Germany). Breath-by-breath end-tidal CO_2 ($etCO_2$) levels and respiration rate were monitored continuously through a face mask connected to an infrared CO_2 analyzer (Gambro, Enström, Sweden).

Subjects rested in the recumbent position for 10 min to establish preexercise baseline values; subjects breathed spontaneously during this period. Subjects then completed one set of their 10 RM at a frequency of 10 repetitions/30 s (0.33 Hz). Subjects were instructed to exhale during the concentric contraction and inhale during the eccentric contraction. Immediately after the completion of the set, subjects stood for 10 min and rated their perception of lightheadedness (subject perceived rating, SPR) at 30 s, 60 s, 5 min, and 10 min using the following scale: 1 = no lightheadedness; 2 = mild lightheadedness; 3 = moderate lightheadedness; 4 = severe lightheadedness; and 5 = impending faint (8). Subjects then returned to the recumbent position for a 5-min recovery period. Subjects breathed spontaneously during the stand and subsequent recovery period. Each subject completed the experimental session twice, once under EUH and once under DEH conditions in a counterbalanced design so that five subjects received EUH first and five subjects received DEH first.

Data acquisition and analysis. Data were sampled at 500 Hz and recorded to computer with data-acquisition software (WINDAQ, Dataq Instruments, Akron, OH). Data were then analyzed using a biomedical analysis software program (WinCPRS, Absolute Aliens, Turku, Finland). Due to a noticeable anticipation period immediately prior to commencement of the leg-press exercise, data from the first 3 min of the 10-min baseline were analyzed to establish baseline values. The entire 30 s of exercise data were analyzed for the exercise time point. To coincide with the subject's SPR scores, data were analyzed in two 30-s segments during the first minute of stand (0–30 and 30–60 s), and in 3-min segments at 5 min (2–5 min) and 10 min (7–10 min) following initiation of the stand after exercise. R-waves generated from the ECG were detected and marked at their occurrence in time. Systolic and diastolic pressures (SAP, DAP) and velocities were marked from the arterial pressure and cerebral blood velocity waveforms. MAP and mean MCAv were automatically calculated as the area under the arterial pressure and cerebral blood velocity waveforms, via the WinCPRS software. Beat-to-beat stroke volume (SV) and cardiac output (Q) were estimated using the pulse contour method (18) and total peripheral resistance (TPR) was calculated by dividing MAP by Q. R-R intervals (RRIs), arterial pressures, and cerebral blood velocities were analyzed in both the time and frequency domains. To express RRIs, arterial pressures and cerebral blood velocities as a function of frequency, nonequidistant data were interpolated and then resampled at 4 Hz for spectral analysis (11). Data were then passed through an impulse response filter with a cutoff frequency of 0.4 Hz and submitted to a Fourier transform to generate power spectra. Low-frequency (LF) oscillations in MAP and mean MCAv were calculated within the frequency range of 0.07–0.2 Hz (46), while LF oscillations in RRI and SAP were calculated with the frequency range of 0.04–0.15 Hz. A cross-spectrum analysis of the individual autospectra derived from MAP and mean MCAv was used to quantify cerebral regulatory capacity, and between RRIs and SAP to quantify cardiac baroreflex sensitivity. The coherence function derived from the cross-spectral analyses was calculated to assess the linear relationship between MAP and mean MCAv, and between RRI and SAP. The transfer function was also calculated to assess beat-to-beat system gain within the same frequency ranges (45). A representative example of time-to-frequency domain data conversion is shown in Fig. 1 for assessment of cerebral autoregulation.

Statistical analysis. All data were analyzed with commercially available statistical software (SigmaPlot, Systat Software). We tested for differences among the mean values of interest between baseline and exercise for each hydration condition using a two-way repeated-measures ANOVA. For assessment of differences among the mean values of interest between baseline and stand following exercise, two (hydration condition; EUH and DEH) by five (time; baseline, 30 s, 60 s, 5 min, and 10 min of standing) factorial ANOVAs for repeated measures were implemented for time domain data. Similarly, two (hydration condition; EUH and DEH) by three (time; baseline, 5 min, and 10 min) repeated-measures ANOVAs were used for frequency domain data. Student-Newman-Keuls post hoc tests were conducted to determine differences between groups. Exact *P* values are presented to reflect the probability that the observed response represented chance effects, given random sampling variability. Data are presented as means ± SE unless specified otherwise.

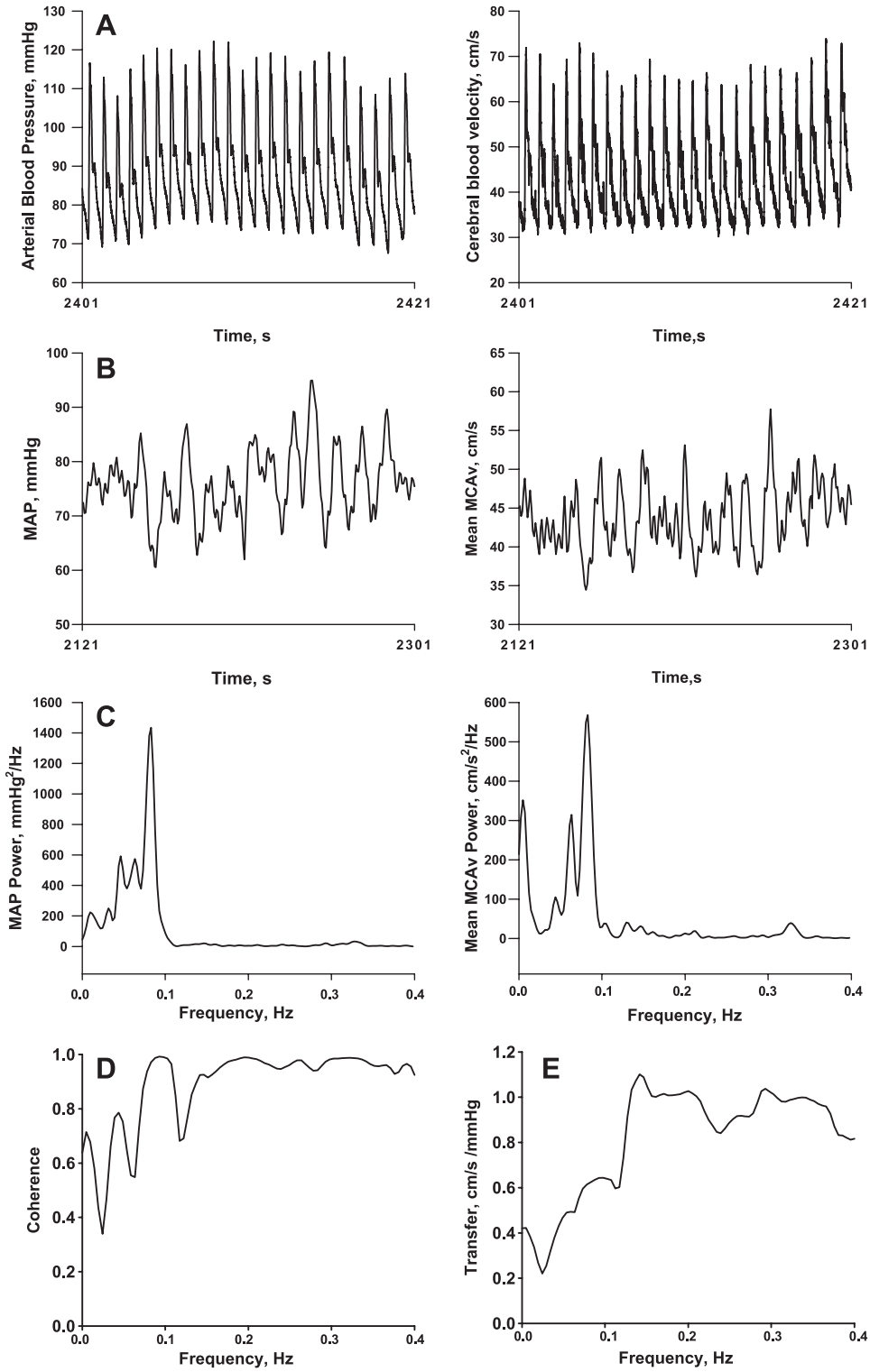

Fig. 1. Representative tracings of arterial pressure and cerebral blood velocity from a dehydrated (DEH) subject during stand (*A*); 3-min tracings of mean arterial pressure (MAP) and mean middle cerebral artery velocity (MCAv) derived from continuous waveforms (*B*); *C* shows conversion of time-domain variables to the frequency domain using Fourier transform; cross-spectral associations between MAP and mean MCAv are displayed as coherence in *D* and transfer function gain in *E*.

RESULTS

Hydration. Furosemide and fluid restriction resulted in a 2.7 ± 0.3% ($P < 0.01$) reduction in body mass, a 6.7 ± 1.4% ($P = 0.006$) increase in Hct, and a 7.1 ± 0.9% ($P = 0.001$) increase in Hb, resulting in a calculated decrease in both blood (6.5 ± 0.9%) and plasma (11.2 ± 1.4%) volume (both $P < 0.01$).

Baseline responses to dehydration. Hemodynamic responses to DEH are shown in Table 1. DEH reduced SV, resulting in a compensatory increase in HR to maintain Q. DEH did not alter MAP ($P = 0.99$), mean MCAv ($P = 0.44$), $etCO_2$ ($P = 0.55$) or respiratory rate at baseline ($P = 0.31$).

Exercise responses. Resistive leg press exercise elicited increases of MAP and mean MCAv under both hydration

Table 1. *Hemodynamic responses to dehydration and exercise*

	Baseline		Exercise	
	EUH	DEH	EUH	DEH
HR, beats/min	71 ± 4	83 ± 6*	124 ± 5†	127 ± 6†
SV, ml	73 ± 2	59 ± 3*	76 ± 6	73 ± 3†
Q, l/min	5.2 ± 0.3	5.0 ± 0.3	9.7 ± 0.7†	9.3 ± 0.3†
MAP, mmHg	93 ± 1	93 ± 3	124 ± 5†	128 ± 6†
Mean MCAv, cm/s	61 ± 2	58 ± 3	73 ± 3†	69 ± 4†
TPR, mmHg·l^{-1}·min	19.1 ± 1.5	20.8 ± 1.2	14.5 ± 2.5	18.2 ± 1.7
$etCO_2$, %	4.7 ± 0.1	4.6 ± 0.2	5.3 ± 0.2†	5.2 ± 0.2†
RR, breaths/min	15 ± 1	16 ± 1	20 ± 1†	20 ± 0.4†

Values are means ± SE; EUH, euhydration; DEH, dehydration; HR, heart rate; SV, stroke volume; Q, cardiac output; MAP, mean arterial pressure; mean MCAv, mean middle cerebral artery velocity; TPR, total peripheral resistance; $etCO_2$, end-tidal CO_2; RR, respiratory rate. *$P \leq 0.05$ between hydration conditions; †$P \leq 0.05$ compared with baseline within hydration condition.

conditions ($P \leq 0.001$) (Table 1). Similarly, exercise increased HR under both hydration conditions and SV during DEH, resulting in elevations in Q that were not distinguishable between EUH and DEH. Because breathing rate was synchronized to the controlled leg press frequency, respiratory rate and $etCO_2$ were not different between hydration conditions ($P \geq 0.41$). Average increases of both MAP and mean MCAv were accompanied by wide oscillations associated with individual leg press repetitions as shown in Fig. 2.

Time domain responses during standing after exercise. Subjects reported greater symptoms during DEH compared with EUH during the first 30 s of standing after exercise (DEH 2.1 ± 0.2 vs. EUH 1.5 ± 0.1; $P = 0.05$); reported symptoms were not different between groups throughout the remaining period of the stand (Fig. 3). One subject began to cough in the EUH condition ~5.5 min into the stand and was returned to the recumbent position to remove the facemask. For this reason, all comparisons are made with nine subjects for the 10-min time point.

The HR, SV, and Q responses to standing under the two hydration conditions are presented in Fig. 4. At baseline, DEH and EUH were distinguishable with a $P \leq 0.05$ for both HR and SV (as indicated in Table 1). Standing following exercise in the DEH condition resulted in a progressive reduction in SV that fell below baseline levels at the 5- and 10-min time points. In the EUH condition, however, SV initially increased by ~7% at the 30-s and 60-s time points, and then fell below baseline by the end of the 10-min stand. HR responses under the two hydration conditions reflect these different SV trajectories; during DEH, HR initially increased during the first 60 s of stand, then fell at the 5- and 10-min time points, but was still elevated above the baseline level throughout the stand period. During EUH, HR fell from the exercise level throughout the stand period, but was also above the baseline level at each time point. Differences in SV responses resulted in a distinguishable Q difference between hydration conditions for the first 60 s of stand ($P \leq 0.01$). There was a progressive reduction in Q during stand under both conditions, reaching baseline levels by the 5-min time point.

Hydration condition did not affect the MAP response during the initial phase of stand following exercise (Fig. 5). MAP fell below baseline levels at the 30-s time point under both hydration conditions ($P < 0.01$) and then recovered to baseline levels for EUH ($P = 0.51$) but not for DEH ($P = 0.02$) 60 s into stand. MAP was similar to baseline throughout the rest of the stand period under the EUH condition, but was slightly lower than baseline at the 10-min time point for DEH ($P = 0.057$). The pattern of blood pressure responses was not directly transferred to MCAv responses, as presented in Fig. 5. Unlike MAP, mean MCAv remained lower for DEH than EUH throughout the stand. Mean MCAv decreased for both hydration conditions 30 s following stand, falling below baseline for DEH ($P = 0.02$). As with MAP, mean MCAv recovered 60 s into stand, resulting in values well above baseline under both conditions. Mean MCAv again fell below baseline at the 5- and 10-min time points during DEH ($P \leq 0.01$), and was similar to baseline values during EUH at these time points ($P \geq 0.08$).

TPR, respiration rate, and $etCO_2$ data are presented in Table 2. During stand following exercise, TPR remained below the baseline level in both the EUH and DEH condition, except for the 10-min time point under DEH where TPR returned to baseline; TPR responses during the stand were not different

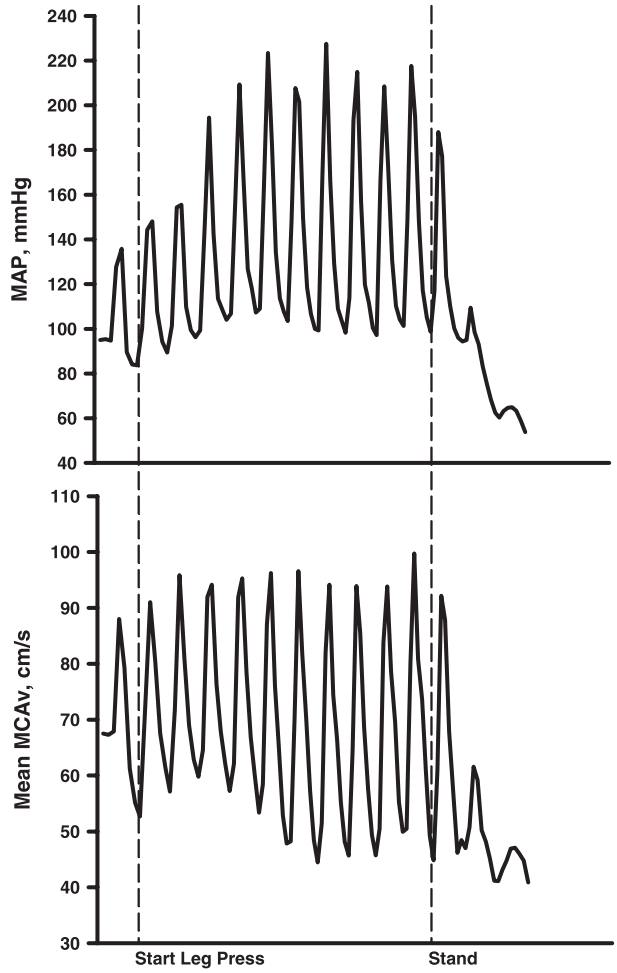

Fig. 2. Representative tracing from a euhydrated (EUH) subject of MAP and mean MCAv during heavy resistance exercise. The first oscillation is due to the initial concentric contraction before the exercise protocol commenced. Dashed vertical lines indicate the start and the end of 10 repetitions of leg press exercise. The oscillation after the second vertical dashed line represents the stand after exercise followed by the rapid reduction in both MAP and mean MCAv. Cross-spectral associations between the two signals resulted in a coherence value of 0.99 at the frequency of 0.33 Hz (frequency of repetitions).

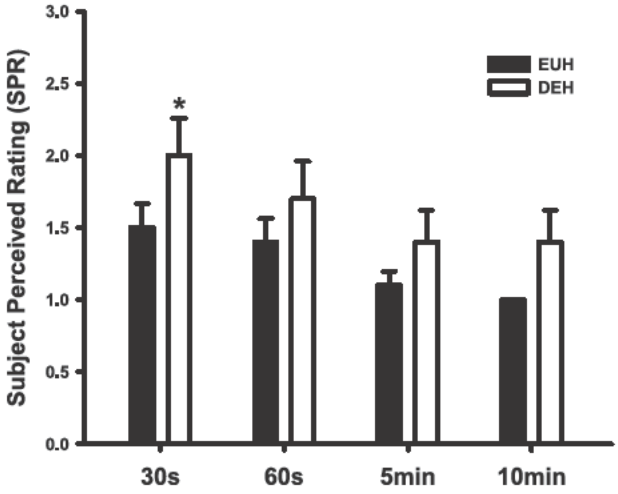

Fig. 3. Subject perceived rating (SPR) of orthostatic symptoms are shown during standing after leg-press exercises. Subjects used the following scale: *1*) no lightheadedness, *2*) mild lightheadedness, *3*) moderate lightheadedness, *4*) severe lightheadedness, and *5*) impending faint. *$P = 0.05$ between DEH and EUH.

between hydration conditions. Respiration rates decreased to baseline levels throughout standing after exercise, and there was no difference between hydration conditions. Compared with baseline, $etCO_2$ was higher during the first 60 s of stand, but returned to baseline values 5 and 10 min into the stand, with no differences between hydration conditions at any time point.

Frequency domain responses during stand after exercise. LF MAP and mean MCAv oscillations derived from the Fourier transform analysis are shown in Fig. 6. Both MAP ($P = 0.057$) and mean MCAv ($P = 0.05$) LF power were higher under the DEH condition compared with EUH at baseline. This difference between hydration conditions persisted throughout the stand, except for mean MCAv LF at the 10-min time point ($P = 0.16$). Importantly, MAP LF increased in the DEH condition over time, and deviated from baseline with a probability value of 0.05 by the end of the 10-min stand. Coherence between MAP and mean MCAv at baseline was higher ($P = 0.01$) with DEH (0.81 ± 0.04) than EUH (0.66 ± 0.05) but was indistinguishable between hydration conditions throughout the 10-min stand (0.82 ± 0.04 and 0.81 ± 0.06 at 5 and 10 min for EUH; 0.83 ± 0.05 and 0.84 ± 0.02 at 5 and 10 min for DEH; $P \geq 0.61$). The assessment of beat-to-beat system gain via the transfer function yielded similar results, showing no difference between the hydration conditions at baseline (EUH: 0.84 ± 0.06 $cm \cdot s^{-1} \cdot mmHg^{-1}$; DEH: 0.84 ± 0.07 $cm \cdot s^{-1} \cdot mmHg^{-1}$; $P = 0.99$) and throughout the stand (0.91 ± 0.05 and 0.89 ± 0.08 $cm \cdot s^{-1} \cdot mmHg^{-1}$ at 5 and 10 min for EUH; 0.79 ± 0.10 and 0.83 ± 0.10 $cm \cdot s^{-1} \cdot mmHg^{-1}$ at 5 and 10 min for DEH; $P \geq 0.21$). Coherence between RRI and SAP was indistinguishable at baseline and throughout the stand phase between hydration conditions ($P \geq 0.22$). SAP-RRI transfer function gain was similar between hydration conditions ($P \geq 0.25$), except at the 10-min time point of stand, where gain was higher in the EUH condition (EUH: 8.0 ± 1.9 ms/mmHg; DEH: 4.8 ± 1.3 ms/mmHg; $P = 0.03$).

DISCUSSION

We studied the influence of voluntary dehydration with fluid restriction and furosemide ingestion on hemodynamic and cerebrovascular responses to standing after heavy resistance exercise. Our results indicate that *1*) during the first 30 s of standing after exercise, subjects report greater, but still only mild, symptoms of lightheadedness during DEH compared with EUH; *2*) reductions of mean MCAv are greater for DEH than EUH during standing immediately after exercise; and *3*) LF MAP and mean MCAv oscillations increase with DEH, and these increases persist throughout standing after resistance exercise. These findings support two conclusions: *1*) voluntary dehydration represents a robust challenge for maintenance of MCAv in the upright posture after heavy resistance exercise; and *2*) despite greater reductions in cerebral blood velocity, dehydration on the order of ~10% is tolerated well and poses no serious challenge to maintenance of upright posture after heavy resistance exercise. This observation may be related to a protective influence of increases in oscillations of arterial pressure and cerebral blood velocity after DEH.

Hydration. Dehydration induced with voluntary fluid restriction and oral administration of 40 mg furosemide reduced plasma volume by 11.2%, blood volume by 6.5%, and body mass by 2.7%. These results are comparable to other studies

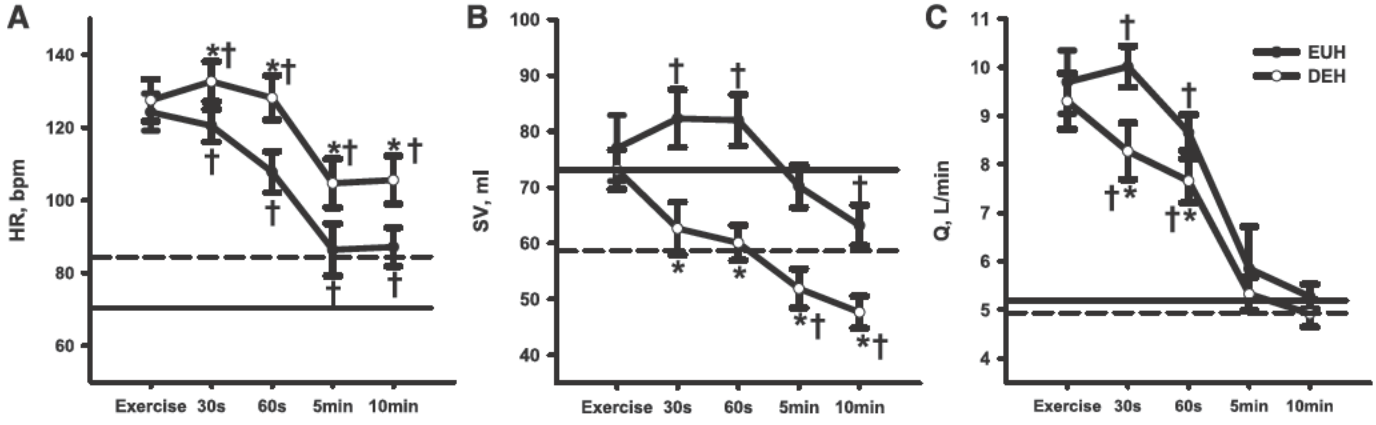

Fig. 4. Hemodynamic responses to stand following heavy resistance exercise during EUH and DEH. Baseline is represented by solid (EUH) and dashed (DEH) horizontal lines. The exercise value is derived from the 30-s leg press exercise; 30-s averages for acute phase of standing after heavy leg press exercise at 30 s (0–30 s) and 60 s (30 s-60 s); and 3-min averages at 5-min and 10-min of stand. HR, heart rate; SV, stroke volume; Q, cardiac output. *$P \leq 0.05$ between hydration conditions; †$P \leq 0.05$ compared with baseline within hydration condition.

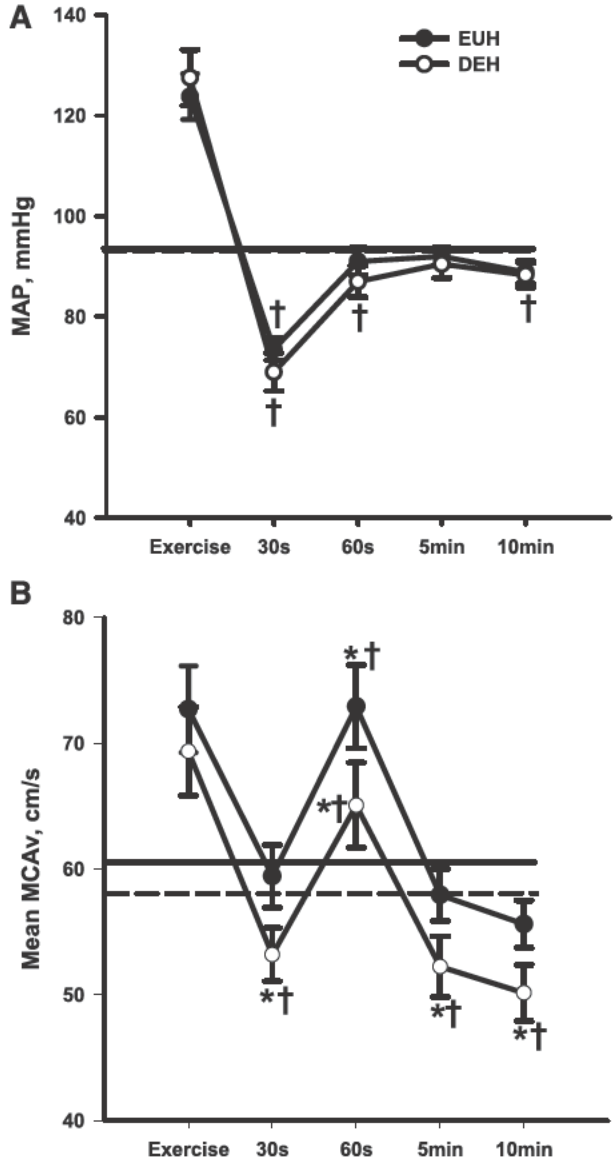

Fig. 5. MAP and mean middle MCAv responses to stand following heavy resistance exercise during EUH and DEH. Baseline is represented by solid (EUH) and dashed (DEH) horizontal lines. The exercise value is derived from the 30-s leg press exercise; 30-s averages for acute phase of standing after heavy leg press exercise at 30 s (0–30 s) and 60 s (30 s–60 s); and 3-min averages at 5 min and 10 min of stand; $*P \leq 0.05$ between hydration conditions; $\dagger P \leq 0.05$ compared with baseline within hydration condition.

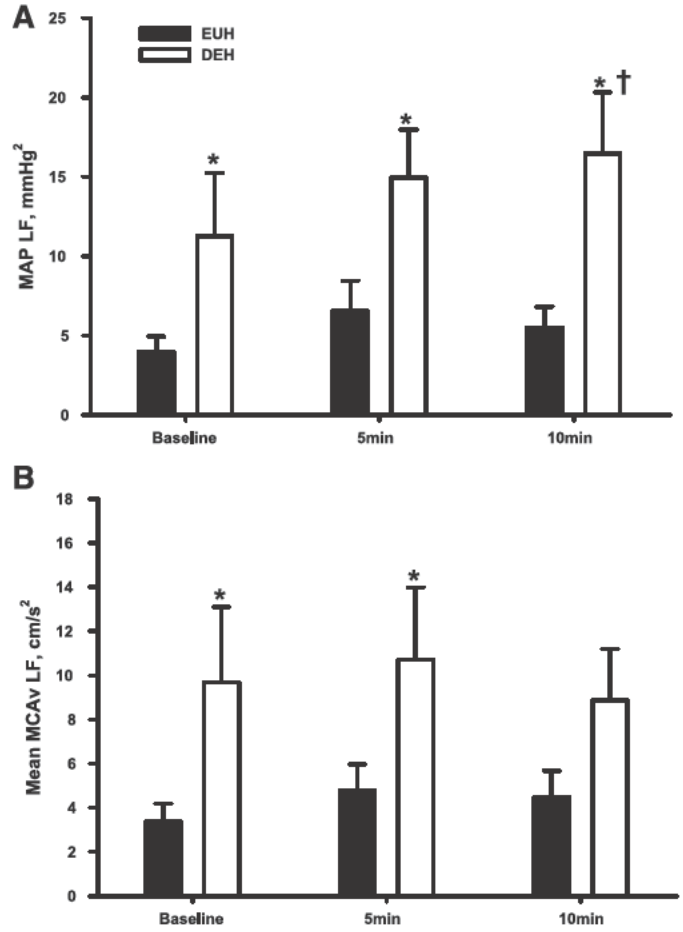

Fig. 6. Low-frequency (LF) oscillatory power (0.07–0.2 Hz) for MAP and mean MCAv at baseline and during the 10-min stand following heavy resistance exercise following EUH and DEH. Three minutes of data are used at each time point. $*P \leq 0.057$ between hydration conditions; $\dagger P \leq 0.05$ compared with baseline within hydration condition.

utilizing similar pharmacologically induced dehydration strategies (4, 35, 44), and passive dehydration of athletes with heat (i.e., sauna) exposure (37). Others have shown that dehydration of the magnitude we report challenges autonomic compensatory mechanisms designed to ensure the maintenance of adequate blood pressure and cerebral perfusion for subjects in the upright posture (5, 6).

Exercise responses. Heavy resistance exercise poses unique challenges to the maintenance of cerebral perfusion due to the rapid and large increases in arterial pressures; in fact, MacDougall et al. (25) documented arterial pressures as high as 450/380 mmHg in healthy subjects during heavy leg press exercise. In the present study, recumbent heavy leg press exercise only increased arterial pressure to about 167/103 mmHg on average, which is similar to studies that utilize leg resistance exercise (22, 30, 34). These levels, however, may still pose a challenge to cerebral regulatory mechanisms (14,

Table 2. *Hemodynamic responses during stand after heavy resistance exercise*

	30 s		60 s		5 min		10 min	
	EUH	DEH	EUH	DEH	EUH	DEH	EUH	DEH
TPR, mmHg·l^{-1}·min	7.9 ± 0.5†	9.2 ± 0.7†	11.0 ± 0.6†	12.2 ± 0.8†	16.2 ± 0.9†	17.9 ± 1.0†	17.0 ± 1.0†	18.7 ± 1.0
$etCO_2$, %	6.0 ± 0.2†	5.7 ± 0.3†	6.4 ± 0.2†	6.2 ± 0.2†	4.7 ± 0.1	4.6 ± 0.1	4.6 ± 0.1	4.3 ± 0.1
RR, breaths/min	18 ± 2	16 ± 2	17 ± 1	17 ± 2	17 ± 1	16 ± 1	16 ± 1	16 ± 2

Values are means ± SE. $\dagger P < 0.05$ compared with baseline within hydration condition.

29, 34). In the present study, mean MCAv increased to the same extent in the DEH and EUH conditions during leg press exercise, following the increases in MAP. In fact, despite differences in baseline blood volume (and subsequently SV and HR), the hemodynamic and cerebral blood velocity profiles of subjects performing heavy resistance exercise were similar between hydration conditions.

Hemodynamics during standing after exercise and symptoms of lightheadedness. Carter et al. (5) have shown that dehydration causes arterial pressures and MCAv to fall acutely upon assumption of upright posture, but return to baseline levels within ~30 s. The magnitude of reduction in MCAv with orthostasis is greater after subjects have been dehydrated by either heat stress (5) or fluid restriction and diuretics (35). Furthermore, Romero and Cooke (34) demonstrated an exacerbation of the reduction in MCAv in normovolemic individuals after leg press exercise with prior hyperventilation. In the present study, while arterial pressure responses were similar between hydration conditions, mean MCAv was consistently lower for DEH than EUH for the entire 10 min of standing after exercise, and was below baseline values for DEH at 30 s, 5 min, and 10-min of the stand. Symptoms of lightheadedness are related to decreased cerebral perfusion and oxygenation (23, 43), suggesting that the reported increase in our subjects' perception of lightheadedness with DEH in the acute phase of stand (30 s) might be a consequence of the initial drop in mean MCAv below a "symptomatic threshold" level (Fig. 5). However, despite lower initial reductions of MCAv, symptoms reported by DEH subjects were classified as mild, all subjects completed the 10-min stand without further symptoms of cerebral hypoperfusion, and no subject experienced impending syncope. Contrary to our hypothesis, orthostatic performance was not strongly affected by DEH. The findings of the present study are supported by Thomas et al. (40), who found there was no relationship between either symptoms, or acute, transient reductions in MCAv and MAP upon standing and orthostatic tolerance to combined head-up tilt and lower-body negative pressure (LBNP).

We observed the typical progressive increase in TPR expected during standing after heavy resistance exercise, reflecting a sympathetically mediated vasoconstriction in both EUH and DEH conditions. However, the DEH condition failed to elevate TPR to a greater magnitude than that measured during EUH. As such, the primary compensatory mechanism that subjects relied on during standing and DEH in the present investigation was a greater elevation in HR compared with their EUH state. This observation is not without precedent. The contribution of beta adrenergic-induced elevations in HR as a primary mechanism for maintenance of arterial blood pressure and orthostatic stability in healthy subjects is supported by the observation that tolerance to central hypovolemia is reduced even in the presence of maximal increases in TPR when the tachycardic response is inhibited by propranolol (9). The results of the present study reinforce the importance of autonomically mediated cardiac chronotropic responses in maintaining orthostatic stability in DEH as well as EUH states.

A linear relationship between Q and cerebral blood flow under conditions of either orthostasis or exercise has been previously reported. Van Lieshout et al. (43) observed that mean MCAv was decreased in association with the reduction in Q that occurs when subjects move from supine to standing positions, and Ogoh et al. (27) confirmed that mean MCAv and Q were related linearly, both at rest and during exercise. In the present study, while Q was statistically lower in the DEH condition at the 30-s and 60-s time points, it was still well above baseline values and never fell below baseline for the entire 10 min of stand, so it is unlikely that a reduction in Q accounts for the greater reduction in MCAv with DEH.

Hyperventilation and subsequent decreases in arterial CO_2 elicit cerebral vasoconstriction and a reduction in cerebral flow (2, 3, 26). However, the pattern of $etCO_2$ responses was similar between hydration conditions and therefore cannot account for the exacerbated fall in MCAv observed during DEH. While the exaggerated reduction of mean MCAv during standing after exercise with DEH is most likely associated with lower circulating plasma volume, the precise mechanism is unclear considering the pattern of response of arterial pressure, Q, and $etCO_2$.

Frequency-domain assessment of cerebral regulation. Mean MCAv decreased during the prolonged phase of the stand to below baseline levels in DEH subjects. Despite this, dehydrated subjects did not report greater symptoms of lightheadedness. In an attempt to explain this observation, we assessed the magnitude of LF oscillations in MAP and mean MCAv as well as their coherence within the frequency range considered to encompass effective cerebrovascular control (0.07- 0.2 Hz). DEH increased the absolute magnitude of LF MAP and MCAv oscillations at rest and during the 10-min stand (Fig. 6), and increased coherence between these variables at baseline, while transfer function gain was identical between conditions at each time point. We propose that the elevated baseline coherence and increase in LF MAP and mean MCAv oscillations at baseline and during stand in the DEH condition may be indicative of altered cerebral regulation that may act as a protective compensatory mechanism to maintain cerebral perfusion, despite absolute mean MCAv falling below baseline values (Fig. 5). As such, the lower cerebral blood velocities recorded during DEH may have been sufficient to maintain adequate cerebral perfusion due to the oscillatory pattern of MAP and, subsequently, MCAv.

Increases in hemodynamic variability have traditionally been interpreted as being indicative of imminent syncope during orthostatic stress (15, 24, 46). There is evidence, however, supporting the alternative viewpoint as increases in mean MCAv oscillations have been associated with improved tolerance during a number of protocols that elicit central hypovolemia (17, 19, 31, 32, 35). In two studies, Rickards et al. have shown that increases in MCAv LF oscillations (exogenous and endogenous) are associated with increased tolerance to central hypovolemia induced via LBNP (31, 32). In the first of these studies, increases in the power of MCAv LF oscillations was induced by breathing through an inspiratory threshold device and was associated with an improvement in LBNP tolerance within the same subjects (32); subsequent analysis has revealed that the duration, amplitude and slope of upstroke of individual oscillations was increased compared with the control condition (33). We suspect that these alterations in waveform characteristics may optimize cerebral blood flow and delivery of oxygen to the cerebral tissues. In the second study, Rickards et al. (31) showed that subjects with higher tolerance to central hypovolemia were endogenously able to increase the power of MCAv LF oscillations; subjects with lower tolerance did not demonstrate increases in MCAv LF oscillations and exhibited presyncopal symptoms at lower LBNP levels, suggesting an

earlier compromise of cerebral perfusion. In addition, Romero et al. (35) have reported greater reductions in mean MCAv during upright tilt with dehydration that were accompanied by higher MCAv LF oscillations. In this study, MCAv decreased below EUH levels upon standing and was accompanied by parallel increases in LF oscillations. As subjects did not report any symptoms of reduced cerebral perfusion, we speculate that the oscillations may have conferred a similar protective effect to that observed previously. Other studies have also reported an increase in arterial pressure LF oscillations associated with increased tolerance to acute hypovolemic stress, including head-up tilt (19), and combined head-up tilt and LBNP (17). Importantly, Kamiya et al. (19) demonstrated a reduction in MAP LF oscillations coincident with the onset of hypotension in subjects who became syncopal during head-up tilt, while MAP LF oscillations remained elevated in subjects in whom MAP was maintained and who did not show presyncopal symptoms. While oscillations in cerebral blood velocity were not reported in these latter two studies, we speculate that oscillations in arterial pressure would be transferred to the cerebral vasculature as in the present study.

The mechanism underlying the increase in LF oscillations may be multifactorial, including impairment of baroreflex sensitivity and/or cerebral autoregulation, the influence of breathing, voluntary muscle contractions, or oscillatory sympathetic discharge. Increases in the variability of arterial pressure and cerebral blood velocity have been associated with reduced buffering capacity of baroreflex and cerebral autoregulatory mechanisms (39, 41, 46). In the present study, however, transfer function gain between MAP and mean MCAv (index of cerebral autoregulation) was similar at each time point between hydration conditions, and the only difference in cardiac baroreflex sensitivity occurred at the 10-min time point of stand, indicated by higher SAP-RRI transfer function gain in the EUH condition compared with DEH. These observations argue against a direct link between changes in baroreflex sensitivity and/or cerebral autoregulation and LF oscillations, at least under conditions of moderate orthostatic stress. Breathing at frequencies within the range of interest (i.e., 0.07–0.2 Hz; 4.2–12 breaths/min) could entrain both arterial pressure and cerebral blood velocities to oscillate at the same frequency. On average, however, subjects were breathing above 12 breaths/min (0.2 Hz) during the standing phase of the protocol, and there was no difference in breathing frequency between hydration conditions. Likewise, while cyclical muscle contractions within this frequency range could have a similar effect on the oscillatory pattern of arterial pressure and cerebral blood velocity, subjects were instructed to remain as still as possible and to avoid conscious muscle contractions during the standing period. In addition, LF oscillations in sympathetic activity increase with central hypovolemia such as LBNP (12, 19) and head-up tilt (10), and coherence between muscle sympathetic nerve activity (MSNA) and arterial pressure increases as the severity of hypovolemia progresses (12). While we did not measure MSNA in this study, Kimmerly and Shoemaker (20) documented a 23% increase in resting MSNA after administration of the diuretic spironolactone that resulted in plasma and blood volume reductions similar to those we observed in the present study; while not reported, we speculate that MSNA LF oscillations increased coincidently (12, 16, 19). In this study, HR was higher at baseline for DEH compared with EUH, suggesting a generalized sympathetic activation in response to dehydration (Table 1). It is therefore possible that at baseline and during stand, DEH elicited a greater increase in MSNA LF oscillations that were directly transferred to the arterial vasculature, potentially accounting for the higher LF oscillations in MAP and mean MCAv observed in the DEH condition. We cannot speculate on whether or not proposed increases in sympathetic traffic with DEH may be transferred to the cerebrovasculature; the potential influences of changes in sympathetic activity on cerebral blood flow are equivocal (42).

Study limitations. We used furosemide plus fluid restriction to induce dehydration, and we did not include a control group who dehydrated naturally with fluid restriction alone. This leaves open the possibility that furosemide might have off-target effects in the cerebral vasculature. Although this possibility has not been tested experimentally in the intact cerebrovasculature, furosemide does not influence vasoactivity of arterial vascular smooth muscle of the forearm in humans (28); the same may or may not apply to the cerebral vessels.

We recognize that transcranial Doppler ultrasound measures flow velocity, and not flow. Determination of velocity during an experimental perturbation depends importantly on the angle of insonation. In our study, we used headgear designed to maintain a constant angle during measurement, but we did not verify the constancy of the insonation angle for measurements performed on separate days. However, the consistency of the reduction in mean MCAv across each subject with DEH and standing indicates that this was not just a chance effect due to day-to-day differences in the angle of insonation.

Conclusions. Inadequate hydration is a serious concern for athletes. We hypothesized that inadequate hydration may uniquely impact weightlifting athletes by overwhelming cerebral regulatory capacity. Indeed, with dehydration, autonomic compensatory mechanisms may not be rapid enough to prevent mean MCAv from falling below a symptomatic threshold during the acute phase of standing, resulting in mild and transient symptoms of cerebral hypoperfusion. During the prolonged phase of standing after exercise, the consistently lower MCAv experienced with DEH was accompanied by increases in LF MAP and mean MCAv oscillations. It is possible that these exaggerated LF oscillations represent protective mechanisms that act to maintain cerebral perfusion and limit symptoms of impending presyncope when absolute cerebral blood flow is reduced. As symptoms were transient and quickly resolved, and tolerance to orthostasis was not affected, these findings suggest that the degree of hypovolemia we induced in our subjects was well tolerated and does not present a risk for athletes who may dehydrate before resistance exercise.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

Author contributions: G.M., S.A.R., and W.H.C. conception and design of research; G.M., S.A.R., and W.H.C. performed experiments; G.M., S.A.R., and W.H.C. analyzed data; G.M., S.A.R., C.A.R., K.L.R., V.A.C., and W.H.C. interpreted results of experiments; G.M. and W.H.C. prepared figures; G.M., C.A.R., K.L.R., V.A.C., and W.H.C. drafted manuscript; G.M., C.A.R.,

K.L.R., V.A.C., and W.H.C. edited and revised manuscript; G.M., S.A.R., C.A.R., K.L.R., V.A.C., and W.H.C. approved final version of manuscript.

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